CHAPTER I

INTRODUCTION

1.1 Statement of Problem

Poly(L-lactide) or poly(L-lactic acid) (PLLA) (Fig. 1.1) is the one of the most intensively studied biodegradable synthetic polymers in the field of biomedical materials. It has been used as implantable carriers for drug delivery systems [1,2] as well as for surgical repair materials [3-5]. PLLA has good biocompatibility, biodegradability, high mechanical strength, high crystallinity, low hydrophilicity and excellent shaping, molding properties. However, the high crystallinity of the polymer interferes with controlled degradation, and reducing compatibility with soft tissue presenting an obstacle to application as biodegradable soft plastics [6,7]. Many approaches were performed to overcome these problems, for example, the design of stereocopolymer according to enantiomeric composition [8-10], block copolymer with polyether [11-13], branched PLLA [14,15] or blend with other polymer [16,17]. By doing so, adjusting the mechanical property and degradation rate of the polymer are possible.

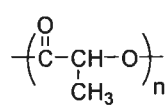

Figure 1.1 Polylactide or poly(lactic acid).

One promising approach to offer changes in the physical and chemical properties of PLLA is to introduce hydrophilic segments by block copolymerization. In general, PLLA is synthesized by ring-opening polymerization of LLA monomers using stannous(II)-2-ethylhexanoate [$Sn(Oct)_2$] as catalyst. The mechanism of polymerization is coordination-insertion mechanism where hydroxy group from a minute amount of alcohol (ROH) or water (H_2O) attack the carbonyl group of LLA, which is coordinated to $Sn(Oct)_2$. Many alcohols such as, benzyl alcohol, 1,4-

butanediol, pentaerythritol, polyglycerine, branched multi-arm poly(ethylene oxide) and hyperbranched polyglycidol with hydroxyl end group were used in the synthesis of linear, branched and star-block copolymers [18-20]. Copolymerization of L-lactide with different types of cyclic monomers, such as lactones or epoxides, provides an important contribution to the already existing materials. The copolymers composed of PLLA and polyether, especially the blocks copolymers, are increasingly considered as worthwhile degradable materials. Actually, introduction of hydrophilic polyether blocks into degradable polyester chains is a mean to make compounds with variable hydrophilicity, degradability, and highly flexible materials.

Polyglycidol (PG), a hyperbranch aliphatic polyether has been used as a source of hydrophilicity. The terminal hydroxyl groups of either linear or hyperbranch PG were reported as a hydrophilic segment and macroinitiator for polymerization of L-lactide [15,20]. In 2003 Poly(L-lactide-*block*-glycidol) (PLLA-*b*-PG) was synthesized by Sunsaneeyametha [20], with molecular weight of 18,300 Da. But the optimization of polymerization condition, detailed polymer structure, and *in vitro* degradation study have not yet carried out.

In this work the synthesis of PLLA-*b*-PG was optimized. The synthesis involved 2 steps: polymerization of glycidol and polymerization of L-lactide by using the hydroxyl groups of PG as initiator cooperating with $Sn(Oct)_2$ catalysis. The method introduced by Sunsaneeyametha was used with some adjustments. The *in vitro* degradation of PLLA-*b*-PG was also monitored in term of change in composition, weight loss, molecular weight, and release of degradation products. It is hypothesized that the copolymer obtained would consist of hydrophilic PG as the core and hydrophobic PLLA as the shell. The copolymer having various L-lactide lengths could be made by adjusting the ratio of LLA and G. The outcome of this work should be a basis for understanding the solubility, thermal properties, hydrophilicity and degradability of the block copolymers, leading to the development of PLLA copolymers for biomedical applications.

1.2 Objective

This work was carried out based on 2 objectives. One was to optimize the synthesis method of poly(L-lactide-*b*-glycidol) block copolymers by ring-opening polymerization of L-lactide using hyperbranched polyglycidol and $Sn(Oct)_2$ as initiating system and characterization of the resulting copolymer. The second aim was to study the degradation behavior of the copolymer obtained.

1.3 Scope of the Investigation

The sequential investigation was carried out as follow.

1. Optimization of the synthesis method of poly(L-lactide-*b*-glycidol) by varying the mole ratio of G:LLA, temperature, polymerization time, and drying agent for PG macromonomer

2. Structure characterization of the resulting polymers by nuclear magnetic resonance spectroscopy (NMR), differential scanning calorimetry (DSC) and molecular weights determination by matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) and gel permeation chromatography (GPC)

3. Degradation behavior of poly(L-lactide-*b*-glycidol). By monitoring the changes in weight loss and molecular weight by weighting and GPC, respectively